WEST Search History

Hide Items | Restore | Clear | Cancel

DATE: Monday, April 24, 2006

Hide?	Set Name	Query	Hit Count
	DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ		
☐	L12	kazlauskas and hydrolase	36
☐	L11	anti-kazlauskas and esterase	0
☐	L10	kazlauskas and esterase	44
☐	L9	kazlauskas esterase	0
☐	L8	anti-kazlauskas and hydrolase	0
☐	L7	anti-kazlauskas and esterase	0
☐	L6	anti-kazlauskas esterase	0
☐	L5	L4 and compound?	28
☐	L4	kazlauskas same lipase	28
☐	L3	kazlauskas	510
☐	L2	kazlauskas lipase	3
☐	L1	anti-kazlauskas lipase	3

END OF SEARCH HISTORY

```
=> file medline hcaplus biosis biotechds embase
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.21       0.21

FILE 'MEDLINE' ENTERED AT 17:09:48 ON 24 APR 2006

FILE 'HCAPLUS' ENTERED AT 17:09:48 ON 24 APR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 17:09:48 ON 24 APR 2006
Copyright (c) 2006 The Thomson Corporation

FILE 'BIOTECHDS' ENTERED AT 17:09:48 ON 24 APR 2006
COPYRIGHT (C) 2006 THE THOMSON CORPORATION

FILE 'EMBASE' ENTERED AT 17:09:48 ON 24 APR 2006
Copyright (c) 2006 Elsevier B.V. All rights reserved.

=> s kazlauskas and lipase
L1          20 KAZLAUSKAS AND LIPASE

=> dup rem l1
PROCESSING COMPLETED FOR L1
L2          10 DUP REM L1 (10 DUPLICATES REMOVED)

=> d l2 1-10 ibib ab

L2   ANSWER 1 OF 10  HCAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2006:366211  HCAPLUS
TITLE:                   Kinetic resolutions with novel, highly
                         enantioselective fungal lipases produced by solid
                         state fermentation
AUTHOR(S):               Nagy, Viviana; Toke, Eniko R.; Keong, Lee Chee;
                         Szatzker, Gabor; Ibrahim, Darah; Omar, Ibrahim Che;
                         Szakacs, Gyoergy; Poppe, Laszlo
CORPORATE SOURCE:        Department of Agricultural Chemical Technology,
                         Budapest University of Technology & Economics,
                         Budapest, Gellert ter 4., H-1111, Hung.
SOURCE:                  Journal of Molecular Catalysis B: Enzymatic (2006),
                         39(1-4), 141-148
                         CODEN: JMCEF8; ISSN: 1381-1177
PUBLISHER:               Elsevier B.V.
DOCUMENT TYPE:           Journal
LANGUAGE:                English
AB   Thirty-eight filamentous fungi cultivated under solid state fermn. (SSF)
     conditions were screened for lipase activity and
     enantioselectivity in kinetic resolns. of racemic secondary alcs.
     (rac-1a-c) by acetylation with vinyl acetate performed in org. solvents.
     Many of the target fungi have not been studied previously for
     lipase/esterase activity and enantioselectivity.  Without special
     enzyme isolation processes, the room temp. (25 .degree.C) dried SSF
     cultures as such were tested in the enantiomer selective
     biotransformations.  The majority of these SSF prepns. proved to be
     effective as enantiomer selective biocatalysts exhibiting high but usual
     enantioselectivities according to the Kazlauskas rule.  However,
     the SSF prepn. of Mucor hiemalis origin acted as a selective anti-
     Kazlauskas catalyst.  The best SSF products were successfully
     applied in preparative scale resolns.

L2   ANSWER 2 OF 10  HCAPLUS  COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER:        2005:1009056  HCAPLUS
DOCUMENT NUMBER:         143:459806
```

TITLE: Enantioselective acylation of rac-2-phenylcycloalkanamines catalyzed by lipases
AUTHOR(S): Gonzalez-Sabin, Javier; Gotor, Vicente; Rebolledo, Francisca
CORPORATE SOURCE: Departamento de Quimica Organica e Inorganica, Universidad de Oviedo, Oviedo, 33071, Spain
SOURCE: Tetrahedron: Asymmetry (2005), 16(18), 3070-3076
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The kinetic resoln. of some 2-(phenyl)cycloalkanamine derivs. was performed by means of aminolysis reactions catalyzed by lipases, with **Kazlauskas'** rule being obeyed in all cases. The size of the ring and the stereochem. of the stereogenic centers of the amines had a strong influence on both the enantiomeric ratio and the reaction rate of these aminolysis processes. **Lipase** B from Candida antarctica (CAL-B) showed excellent enantioselectivity toward trans-2-(phenyl)cyclohexanamine in a variety of reaction conditions (E >150), whereas **lipase** A from C. antarctica (CAL-A) was the best catalyst for the acylation of cis-2-(phenyl)cyclohexanamine (E = 34) and trans-2-(phenyl)cyclopropanamine (E = 9).
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:404364 HCAPLUS
DOCUMENT NUMBER: 143:285878
TITLE: Kinetic resolution of 1-biaryl- and 1-(pyridylphenyl)alkan-1-ols catalysed by the **Lipase** B from Candida antarctica
AUTHOR(S): Kourist, Robert; Gonzalez-Sabin, Javier; Liz, Ramon; Rebolledo, Francisca
CORPORATE SOURCE: Departamento de Quimica Organica e Inorganica, Universidad de Oviedo, Oviedo, 33071, Spain
SOURCE: Advanced Synthesis & Catalysis (2005), 347(5), 695-702
CODEN: ASCAF7; ISSN: 1615-4150
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
AB **Lipase** B from Candida antarctica (CAL-B) catalyzes the highly enantioselective (E > 200) transesterification of some 1-biaryl-2-yl-, -3-yl-, and -4-yl-ethanols and -propan-1-ols, as well as 1-(o-, m-, and p-pyridylphenyl)ethanols, 6, with vinyl acetate, **Kazlauskas'** rule being obeyed in all cases. Meta and para-Substituted substrates were transformed within several hours (conversion degree ranging from 23-50%), reaction rates for propan-1-ol derivs. being slower than those for ethanol derivs. Transesterifications of ortho-substituted alcs. took several days and were accompanied by a chemoenzymic side reaction: the formation of another acetate derived from the hemiacetal between 6 and acetaldehyde coming from vinyl acetate. This side reaction was suppressed in the presence of isopropenyl acetate as acyl donor, conversion degrees for transesterification ranging from 20-40% after ten days (E > 200). The usefulness of (R)-6p as ligand in the asym. addn. of diethylzinc to benzaldehyde was also demonstrated.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2004:386628 HCAPLUS
DOCUMENT NUMBER: 140:387801
TITLE: Lipases with enantioselectivity contrary to the **Kazlauskas** rule and their use in the preparation of enantiomers of alcohols and esters
INVENTOR(S): Bosch, Boris; Meissner, Ruth; Berendes, Frank; Koch,

Rainhard
PATENT ASSIGNEE(S): Bayer Chemicals A.-G., Germany
SOURCE: Eur. Pat. Appl., 22 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1418237	A2	20040512	EP 2003-22590	20031006
EP 1418237	A3	20040630		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
DE 10248166	A1	20040617	DE 2002-10248166	20021016
US 2005153404	A1	20050714	US 2003-686490	20031015

PRIORITY APPLN. INFO.: DE 2002-10248166 A 20021016
OTHER SOURCE(S): MARPAT 140:387801

AB Lipases that show good enantioselectivity even when the alkyl side chains are not substantially different in size, and therefore violate the **Kazlauskas** rule, are described for use in the enantioselective prepn. of esters and alcs. The enzymes can be used in combination with ruthenium complexes that act as racemization catalysts to ensure continual generation of substrate to obtain highly efficient prepn. of the chiral products. CDNAs encoding the enzymes are cloned and characterized. The enzymes were identified by screening 275 candidate lipases identified by searching public sequence databases for **lipase** sequence homologs.

L2 ANSWER 5 OF 10 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-04522 BIOTECHDS
TITLE: Short and efficient chemoenzymatic synthesis of goniothalamin ;
use of **lipase** for production of goniothalamin, which has antitumor, progesterone-antagonist and estrogen-antagonist activities
AUTHOR: GRUTTADAURIA M; LO MEO P; NOTO R
CORPORATE SOURCE: Univ Palermo
LOCATION: Gruttadauria M, Univ Palermo, Dipartimento Chim Organ E Paterno, Viale Sci,Parco Orleans 2, I-90128 Palermo, Italy
SOURCE: TETRAHEDRON LETTERS; (2004) 45, 1, 83-85
ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English

AB AUTHOR ABSTRACT - A high-yielding three-step synthesis of goniothalamin involving an enzymatic kinetic resolution in the presence of vinyl acrylate followed by ring-closing metathesis is discussed. (C) 2003 Elsevier Ltd. All rights reserved.
DERWENT ABSTRACT: The stereoselective synthesis of oxygenated heterocyclic rings such as tetrahydrofurans, tetrahydropyrans, and lactones using **lipase** (EC-3.1.1.3) as biocatalyst are being studied. The chemoenzymatic synthesis of 6-substituted 5,6-dihydro-alpha-pyrone derivatives was studied. In order to develop the approach, goniothalamin was chosen as the target compound. Goniothalamin shows antiprogestagenic and antiestrogenic effects in vivo without toxic effects. The antitumor activity of goniothalamin has been evaluated in vitro showing antiproliferative effects, like tamoxifen, on both MCF-7 and T47-D cell lines. As starting material the racemic allylic alcohol readily obtained from cinnamaldehyde and allylmagnesium bromide was used. As resolving agent for the transesterification reaction vinyl acrylate was chosen. In this way, following the empirical **Kazlauskas** rule, the ester was directly obtained with the correct configuration. The resolution was carried out with PS-C, a Pseudomonas cepacia **lipase** immobilized on ceramic support particles(3 pages)

L2 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:120380 HCAPLUS
DOCUMENT NUMBER: 138:283203
TITLE: On the Mechanism of the Unexpected Facile Formation of meso-Diacetate Products in Enzymatic Acetylation of Alkanediols
AUTHOR(S): Edin, Michaela; Baeckvall, Jan-E.
CORPORATE SOURCE: Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, Stockholm, SE-106 91, Swed.
SOURCE: Journal of Organic Chemistry (2003), 68(6), 2216-2222
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:283203
AB The mechanism of the unexpected facile formation of meso-diacetate previously obsd. in the enzymic resoln. of DL/meso mixts. of 2,4-pentanediol and 2,5-hexanediol with Candida antarctica **lipase** B has been elucidated. It was found that the formation of meso-diacetate proceeds via different mechanisms for the two diols. Enzyme-catalyzed acylation of AcO-d3 labeled (R)-monoacetates of meso-2,4-pentanediol and meso-2,5-hexanediol and anal. of the meso-diacetates obtained show that the former reaction proceeds via intramol. acyl migration while the latter occurs via direct S-acylation of the alc. For the (R)-monoacetate of (R,S)-2,4-pentanediol the intramol. acyl migration was fast and therefore direct S-acylation by the external acyl donor is suppressed. For the hexanediol monoacetate the rate ratio (pseudo E value) between (5R,2R)- and (5R,2S)-5-acetoxy-2-hexanol was exptl. detd. to be kR,R/kR,S = 25, which is about 10-20 times lower than the E value for 2-pentanol and 2-octanol. In a preliminary expt. it was demonstrated that facile acyl migration in the 1,3-diol deriv. can be utilized to prep. syn-1,3-diacetoxynonane (>90% syn) in high enantioselectivity (>99% ee) via a chemoenzymic dynamic kinetic asym. transformation of a meso/DL mixt. of 1,3-nonanediol.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2002:585043 HCAPLUS
DOCUMENT NUMBER: 138:89529
TITLE: CAL-B-catalyzed resolution of some pharmacologically interesting .beta.-substituted isopropylamines
AUTHOR(S): Gonzalez-Sabin, Javier; Gotor, Vicente; Rebolledo, Francisca
CORPORATE SOURCE: Departamento de Quimica Organica e Inorganica, Universidad de Oviedo, Oviedo, 33071, Spain
SOURCE: Tetrahedron: Asymmetry (2002), 13(12), 1315-1320
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:89529
AB Some pharmacol. active amines such as amphetamine, the isomeric o-, m- and p-methoxyamphetamines, 4-phenylbutan-2-amine and mexiletine, as well as their corresponding acetamides, have been prepd. in high yields and with very high enantiomeric excesses. The method consists of the Candida antarctica **lipase** B (CAL-B)-mediated enantioselective acetylation of racemic amines using Et acetate as solvent and acyl donor. The enzyme follows **Kazlauskas'** rule with all amines, (R)-amides being obtained as the major enantiomer in all cases. From the conversion values measured for both enantiomers, it can be deduced that the size of the substituents attached to the stereocenter is responsible for the enantioselectivity and rate of some of these reactions.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 8 OF 10 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2002040827 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11769092
TITLE: [**Lipase**-catalyzed kinetic resolution of 2-substituted cycloalkanols].
2-szubsztitualt cikloalkanolok lipaz-katalizalta kinetikus rezolvalasa.
AUTHOR: Forro E
CORPORATE SOURCE: Szegedi Tudomanyegyetem, Gyogyszerkemiai Intezet, 6701 Szeged, POB 121.
SOURCE: Acta pharmaceutica Hungarica, (2001) Vol. 71, No. 1, pp. 119-26.
Journal code: 0414322. ISSN: 0001-6659.
PUB. COUNTRY: Hungary
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Hungarian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 24 Jan 2002
Last Updated on STN: 28 Jan 2002
Entered Medline: 25 Jan 2002

AB Racemates of cis- and trans-2-cyanocyclopentanol and -cyclohexanol, cis- and trans-2-dialkylaminomethylcyclopentanol, -cyclohexanol and -cycloheptanol and Boc-protected cis- and trans-2-methylhydrazinocyclopentanol and -cyclohexanol were resolved through **lipase** PS (from Pseudomonas cepacia) or Novozym 435 (from Candida antarctica B)-catalysed asymmetric acylation. High enantioselectivity (E > 200) was observed when vinyl acetate was used as acylating agent, with diethyl ether or with diisopropyl ether as solvent. Reaction rates were markedly affected by the solvent and by the quantity of the enzyme. The size of the cycloalkane ring had a clear effect on the rate of enantioselective acylation: the acetylations of the five-membered cycloalcanols proceeded more rapidly than those of the six-membered ones and much more rapidly than those of the seven-membered systems. It can also be concluded that the trans isomers react more rapidly than the cis counterparts, the only exception being found in the case of 2-cyanocyclohexanols. In good correlation with the "**Kazlauskas** rule", in all cases, the (R) enantiomer is acylated faster than the (S) enantiomer, yielding an (R) ester and an (S) alcohol, which products from large-scale experiments were separated by column chromatography. During these studies, a total of 18 racemates of cis- and trans-2-substituted cycloalkanols were resolved by using lipases as catalysts, and 52 enantiomers (50 of them new) were characterized by NMR, elemental analysis and ocasionally MS.

L2 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 1999:594421 HCAPLUS
DOCUMENT NUMBER: 131:337189
TITLE: **Lipase**-mediated resolution of octahydro-3,3,8a-trimethyl-1-naphthalenol, a key intermediate in the total synthesis of lactaranes and marasmanes
AUTHOR(S): Franssen, Maurice C. R.; Jongejan, Hugo; Kooijman, Huub; Spek, Anthony L.; Bell, Roel P. L.; Wijnberg, Joannes B. P. A.; De Groot, Aede
CORPORATE SOURCE: Laboratory of Organic Chemistry, Wageningen University, Wageningen, 6703 HB, Neth.
SOURCE: Tetrahedron: Asymmetry (1999), 10(14), 2729-2738
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 131:337189

AB The bicyclic alc. (1.alpha.,8a.alpha.)-1,2,3,4,6,7,8,8a-octahydro-3,3,8a-trimethyl-1-naphthalenol [(.+-.)-I] was resolved using Candida rugosa **lipase**-mediated esterification with vinyl acetate (E = 72). The abs. configuration of the remaining isomer was detd. by X-ray anal. of its 4-chloro-3-nitrobenzoate. The obsd. stereochem. preference of the enzyme is in line with the rule formulated by **Kazlauskas** et al. [1991]. The resolved alc. is a useful chiral synthon for natural lactarane and marasmane sesquiterpenes.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6

ACCESSION NUMBER: 1996:144582 HCAPLUS
DOCUMENT NUMBER: 124:289303
TITLE: Resolution of a Tetrahydrofuran Ester by Candida rugosa **Lipase** (CRL) and an Examination of CRL's Stereochemical Preference in Organic Media
AUTHOR(S): Franssen, Maurice C. R.; Jongejan, Hugo; Kooijman, Huub; Spek, Anthony L.; Camacho Mondril, Nuno L. F. L.; Boavida dos Santos, M. A. C.; de Groot, Aede
CORPORATE SOURCE: Dep. Org. Chem., Wageningen Agricultural Univ., Wageningen, 6703 HB, Neth.
SOURCE: Tetrahedron: Asymmetry (1996), 7(2), 497-510
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Crude **lipase** from Candida rugosa (CRL) is able to resolve the C3-stereoisomers of the furo[2,3b]furan building block, tetrahydro-2-methoxy-3-furancarboxylic acid Me ester, by alcoholysis using n-butanol in octane. The reaction was not affected by the configuration at C2. The abs. configuration of (2R-cis)-tetrahydro-2-methoxy-3-furancarboxylic acid Me ester was detd. The stereochem. outcome of the reaction was compared to the active site model derived by the group of **Kazlauskas** [Ahmed et al., Biocatalysis 9 (1994), 204]. Evidence was presented for the validity of this model for CRL-catalyzed alcoholysis, esterification and acidolysis reactions in org. media.

=> s l2 and acylation
L3 4 L2 AND ACYLATION

=> d l3 1-4 ibib ab

L3 ANSWER 1 OF 4 MEDLINE on STN

ACCESSION NUMBER: 2002040827 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11769092
TITLE: [**Lipase**-catalyzed kinetic resolution of 2-substituted cycloalkanols].
2-szubsztitualt cikloalkanolok lipaz-katalizalta kinetikus rezolvalasa.
AUTHOR: Forro E
CORPORATE SOURCE: Szegedi Tudomanyegyetem, Gyogyszerkemiai Intezet, 6701 Szeged, POB 121.
SOURCE: Acta pharmaceutica Hungarica, (2001) Vol. 71, No. 1, pp. 119-26.
Journal code: 0414322. ISSN: 0001-6659.
PUB. COUNTRY: Hungary
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Hungarian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200201
ENTRY DATE: Entered STN: 24 Jan 2002
Last Updated on STN: 28 Jan 2002
Entered Medline: 25 Jan 2002

AB Racemates of cis- and trans-2-cyanocyclopentanol and -cyclohexanol, cis- and trans-2-dialkylaminomethylcyclopentanol, -cyclohexanol and -cycloheptanol and Boc-protected cis- and trans-2-methylhydrazinocyclopentanol and -cyclohexanol were resolved through **lipase** PS (from Pseudomonas cepacia) or Novozym 435 (from Candida antarctica B)-catalysed asymmetric **acylation**. High enantioselectivity (E > 200) was observed when vinyl acetate was used as acylating agent, with diethyl ether or with diisopropyl ether as solvent. Reaction rates were markedly affected by the solvent and by the quantity of the enzyme. The size of the cycloalkane ring had a clear effect on the rate of enantioselective **acylation**: the acetylations of the five-membered cycloalcanols proceeded more rapidly than those of the six-membered ones and much more rapidly than those of the seven-membered systems. It can also be concluded that the trans isomers react more rapidly than the cis counterparts, the only exception being found in the case of 2-cyanocyclohexanols. In good correlation with the " **Kazlauskas** rule", in all cases, the (R) enantiomer is acylated faster than the (S) enantiomer, yielding an (R) ester and an (S) alcohol, which products from large-scale experiments were separated by column chromatography. During these studies, a total of 18 racemates of cis- and trans-2-substituted cycloalkanols were resolved by using lipases as catalysts, and 52 enantiomers (50 of them new) were characterized by NMR, elemental analysis and ocasionally MS.

L3 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1009056 HCAPLUS
DOCUMENT NUMBER: 143:459806
TITLE: Enantioselective **acylation** of rac-2-phenylcycloalkanamines catalyzed by lipases
AUTHOR(S): Gonzalez-Sabin, Javier; Gotor, Vicente; Rebolledo, Francisca
CORPORATE SOURCE: Departamento de Quimica Organica e Inorganica, Universidad de Oviedo, Oviedo, 33071, Spain
SOURCE: Tetrahedron: Asymmetry (2005), 16(18), 3070-3076
CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The kinetic resoln. of some 2-(phenyl)cycloalkanamine derivs. was performed by means of aminolysis reactions catalyzed by lipases, with **Kazlauskas**' rule being obeyed in all cases. The size of the ring and the stereochem. of the stereogenic centers of the amines had a strong influence on both the enantiomeric ratio and the reaction rate of these aminolysis processes. **Lipase** B from Candida antarctica (CAL-B) showed excellent enantioselectivity toward trans-2-(phenyl)cyclohexanamine in a variety of reaction conditions (E >150), whereas **lipase** A from C. antarctica (CAL-A) was the best catalyst for the **acylation** of cis-2-(phenyl)cyclohexanamine (E = 34) and trans-2-(phenyl)cyclopropanamine (E = 9).
REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2003:120380 HCAPLUS
DOCUMENT NUMBER: 138:283203
TITLE: On the Mechanism of the Unexpected Facile Formation of meso-Diacetate Products in Enzymatic Acetylation of Alkanediols
AUTHOR(S): Edin, Michaela; Baeckvall, Jan-E.
CORPORATE SOURCE: Department of Organic Chemistry, Arrhenius Laboratory, Stockholm University, Stockholm, SE-106 91, Swed.
SOURCE: Journal of Organic Chemistry (2003), 68(6), 2216-2222
CODEN: JOCEAH; ISSN: 0022-3263
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal

LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:283203
AB The mechanism of the unexpected facile formation of meso-diacetate previously obsd. in the enzymic resoln. of DL/meso mixts. of 2,4-pentanediol and 2,5-hexanediol with Candida antarctica **lipase** B has been elucidated. It was found that the formation of meso-diacetate proceeds via different mechanisms for the two diols. Enzyme-catalyzed **acylation** of AcO-d3 labeled (R)-monoacetates of meso-2,4-pentanediol and meso-2,5-hexanediol and anal. of the meso-diacetates obtained show that the former reaction proceeds via intramol. acyl migration while the latter occurs via direct S-**acylation** of the alc. For the (R)-monoacetate of (R,S)-2,4-pentanediol the intramol. acyl migration was fast and therefore direct S-**acylation** by the external acyl donor is suppressed. For the hexanediol monoacetate the rate ratio (pseudo E value) between (5R,2R)- and (5R,2S)-5-acetoxy-2-hexanol was exptl. detd. to be kR,R/kR,S = 25, which is about 10-20 times lower than the E value for 2-pentanol and 2-octanol. In a preliminary expt. it was demonstrated that facile acyl migration in the 1,3-diol deriv. can be utilized to prep. syn-1,3-diacetoxynonane (>90% syn) in high enantioselectivity (>99% ee) via a chemoenzymic dynamic kinetic asym. transformation of a meso/DL mixt. of 1,3-nonanediol.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:585043 HCAPLUS
DOCUMENT NUMBER: 138:89529
TITLE: CAL-B-catalyzed resolution of some pharmacologically interesting .beta.-substituted isopropylamines
AUTHOR(S): Gonzalez-Sabin, Javier; Gotor, Vicente; Rebolledo, Francisca
CORPORATE SOURCE: Departamento de Quimica Organica e Inorganica, Universidad de Oviedo, Oviedo, 33071, Spain
SOURCE: Tetrahedron: Asymmetry (2002), 13(12), 1315-1320 CODEN: TASYE3; ISSN: 0957-4166
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 138:89529
AB Some pharmacol. active amines such as amphetamine, the isomeric o-, m- and p-methoxyamphetamines, 4-phenylbutan-2-amine and mexiletine, as well as their corresponding acetamides, have been prepd. in high yields and with very high enantiomeric excesses. The method consists of the Candida antarctica **lipase** B (CAL-B)-mediated enantioselective acetylation of racemic amines using Et acetate as solvent and acyl donor. The enzyme follows **Kazlauskas'** rule with all amines, (R)-amides being obtained as the major enantiomer in all cases. From the conversion values measured for both enantiomers, it can be deduced that the size of the substituents attached to the stereocenter is responsible for the enantioselectivity and rate of some of these reactions.
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s Bosch B/au
L4 54 BOSCH B/AU

=> dup rem l4
PROCESSING COMPLETED FOR L4
L5 44 DUP REM L4 (10 DUPLICATES REMOVED)

=> s l5 and (lipase or esterase)
L6 1 L5 AND (LIPASE OR ESTERASE)

=> d l6 ibib ab

L6 ANSWER 1 OF 1 BIOTECHDS COPYRIGHT 2006 THE THOMSON CORP. on STN
ACCESSION NUMBER: 2004-16066 BIOTECHDS
TITLE: New nucleic acid encoding anti-Kazlauskas **lipase** and derived enzymes, useful for stereospecific hydrolysis and synthesis of aralkyl esters, intermediates for pharmaceuticals and plant protection agents; vector-mediated enzyme gene transfer and expression in host cell for recombinant protein production and esterification or hydrolysis reaction
AUTHOR: **BOSCH B**; MEISSNER R; BERENDES F; KOCH R
PATENT ASSIGNEE: BAYER CHEM AG
PATENT INFO: EP 1418237 12 May 2004
APPLICATION INFO: EP 2003-22590 6 Oct 2003
PRIORITY INFO: DE 2002-1048166 16 Oct 2002; DE 2002-1048166 16 Oct 2002
DOCUMENT TYPE: Patent
LANGUAGE: German
OTHER SOURCE: WPI: 2004-378759 [36]
AB DERWENT ABSTRACT:

NOVELTY - Nucleic acid (A) that encodes a polypeptide (B) with the biological activity of an anti-Kazlauskas **lipase** is new. (B) is a 294 amino acid (aa) sequence (SEQ ID: 2).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) DNA construct comprising (A) and a heterologous promoter; (2) vector comprising (A) or the construct of (1); (3) host cell containing (A), the construct of (1) or the vector of (2); (4) methods for preparing (A); (5) (B) as new compounds; (6) methods for preparing (B); (7) method for preparing aralkyl esters of formula (I) by reacting a stereoisomeric mixture of the corresponding alcohol (III) with ester (IV) in presence of (B); and (8) method for preparing aralkanol (IIa) by hydrolysis of a stereoisomeric mixture of esters (Ia) in presence of (B). Ar = 5-14C aryl; R = cyano, 1-12C (halo)alkyl, 5-11C aralkyl or a group A-CO-D, A-D, A-SO2R3, A-SO3W, A-COW or A-N3; A = 1-8C alkylene or is absent; D = R2, OR2, NHR3 or N(R3)2; R2 = 1-8C (halo)alkyl, 6-15C aralkyl or 5-14C aryl; each R3 = 1-8C alkyl, 6-15C aralkyl or 6-14C aryl, or both together complete cyclic amino; W = hydroxy, amino or OM; M = (equivalent of) alkali metal, alkaline earth metal or (organic) ammonium ion; R4 = 1-12C alkyl, 4-10C aryl, 5-11C aryl-alkyl, 2-8C alkenyl or 1-12C haloalkyl; and R1 = 1-12C (halo)alkyl, 5-11C aralkyl or 4-10C aryl.

BIOTECHNOLOGY - Preferred Materials: (A) is DNA (genomic or cDNA) or RNA and is particularly an 885 base pair sequence (SEQ ID: 1), a sequence that encodes (SEQ ID: 2), a fragment of at least 14 base pairs from (SEQ ID: 1), a sequence that hybridizes to, or is complementary with them, a sequence at least 70 % identical with them, or an equivalent of them within the degeneracy of the genetic code. The host cells of (3) are particularly prokaryotes. Preparation: (A) are made by chemical synthesis or synthetic oligonucleotides are prepared and used for PCR amplification or, when labeled, to screen genomic or cDNA libraries derived from plants then selection of clones that hybridize. (B) are made by chemical synthesis or by recombinant expression of (A).

USE - (B) are used as catalysts in esterification or hydrolysis reactions for preparation of enantiomeric aralkanols, or their esters, useful for preparing pharmaceuticals or agricultural chemicals (claimed), also liquid crystal compounds.

ADVANTAGE - (B) has high enantioselectivity for the (S)-ester, even when the steric requirements of the two groups attached to the chiral carbon atom are similar, i.e. it violates the Kazlauskas rule (J. Org. Chem., 56 (1991) 2656). When used with a racemization catalyst, it provides very high conversions.

EXAMPLE - A sequence encoding an anti-Kazlauskas **lipase** was expressed in Escherichia coli. A reaction mixture (in 1 ml toluene) comprising lyophilized culture supernatant (10 %, by weight), 1-(p-tolyl)ethanol as substrate (0.2 M) and vinyl acetate (0.6 M) as acyl donor was incubated for 16 hours at 80 degreesC. Conversion of alcohol to

1-(p-tolyl)ethyl acetate was then 11.7 % with enantiomeric excess of the (S)-ester 44.4 %.(22 pages)

=> d his

(FILE 'HOME' ENTERED AT 17:09:05 ON 24 APR 2006)

FILE 'MEDLINE, HCAPLUS, BIOSIS, BIOTECHDS, EMBASE' ENTERED AT 17:09:48 ON 24 APR 2006

L1 20 S KAZLAUSKAS AND LIPASE
L2 10 DUP REM L1 (10 DUPLICATES REMOVED)
L3 4 S L2 AND ACYLATION
L4 54 S BOSCH B/AU
L5 44 DUP REM L4 (10 DUPLICATES REMOVED)
L6 1 S L5 AND (LIPASE OR ESTERASE)

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	51.03	51.24

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-8.25	-8.25

STN INTERNATIONAL LOGOFF AT 17:16:07 ON 24 APR 2006

=> d l4 1-10 ibib ab

L4 ANSWER 1 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:533899 HCAPLUS
DOCUMENT NUMBER: 129:272197
TITLE: Molecular recognition of sec-**alcohol** **enantiomers** by Candida antarctica **lipase** B
AUTHOR(S): Rotticci, Didier; Haeffner, Fredrik; Orrenius, Christian; Norin, Torbjorn; Hult, Karl
CORPORATE SOURCE: Department of Chemistry, Org. Chem., Royal Institute of Technology, Stockholm, SE-100 44, Swed.
SOURCE: Journal of Molecular Catalysis B: Enzymatic (1998), 5(1-4), 267-272
CODEN: JMCEF8; ISSN: 1381-1177
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A model to explain the enantioselectivity of Candida antarctica **lipase** B towards sec-alcs. based on structure activity and mol. modeling is presented. The origin of the enantioselectivity was found to be due to different modes of binding for the enantiomers. The fast enantiomer places its medium substituent in a site of limited size, the stereoselectivity pocket, whereas the slow enantiomer has to position the large substituent in that same pocket. Our model is in agreement with the 24 different substrates tested. Only substituents smaller than n-Pr can be accommodated by the stereoselectivity pocket. Moreover, important unfavorable electrostatic interactions are involved between this region and halogenated substituents. The former requirement entails a high enantiomeric ratio (E) for sec-alcs. with a medium group smaller than n-Pr and a large group larger than n-Pr. The latter requirement allows high E only for short chain vic-halogenated alcs.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:16511 HCAPLUS
DOCUMENT NUMBER: 132:221632
TITLE: Enantiomeric Synthesis of (S)-2-Methylbutanoic Acid Methyl Ester, Apple Flavor, Using **Lipases** in Organic Solvent
AUTHOR(S): Kwon, Dae Young; Hong, Yun-Jeong; Yoon, Suk Hoo
CORPORATE SOURCE: Food Science and Biotechnology Division, Korea Food Research Institute, Poondang Songnam Kyongki-do, 463-420, S. Korea
SOURCE: Journal of Agricultural and Food Chemistry (2000), 48(2), 524-530
CODEN: JAFCAU; ISSN: 0021-8561
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Enantiomeric selective synthesis of (S)-2-methylbutanoic acid Me ester, which is known as a major apple and strawberry flavor, was performed from racemic 2-methylbutanoic acid using **lipases** in org. solvent. Among 20 **lipases**, **lipase** IM 20 (immobilized **lipase** of Rhizomucor miehei), **lipase** AP (Aspergillus niger), and **lipase** FAP-15 (Aspergillus javanicus) exhibited higher enzymic activities and enantioselectivities and were selected for the synthesis of (S)-2-methylbutanoic acid Me ester. Using these enzymes, the reaction conditions such as temp. and lyophilizing pH were optimized, and kinetic parameters were detd. All of the reactions were performed in isooctane, which was identified as the best reaction media for nonaq. systems. At 20 .degree.C max. enantiomeric excess was obsd., while synthetic activity increased as the temp. increased. Only **lipases** lyophilized at pH 5.5, 6.0, 6.5, and 7.0 showed synthetic activity. In

this pH range, enantioselectivities were not influenced by the lyophilizing pH. The KM,S and KM,R values for ester synthetic activity of **lipase** were 1120 and 1240 mM, resp. Enzyme activity was inhibited by (S)-2-methylbutanamide, and its Ki was calcd. as 84 mM. (S)-2-Methylbutanamide acted as a competitive inhibitor.

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1987:210250 HCAPLUS
DOCUMENT NUMBER: 106:210250
TITLE: Enantiomerically selective pig liver **esterase** -catalyzed hydrolyses of racemic allenic esters
AUTHOR(S): Ramaswamy, Sowmianarayanan; Hui, Raymond A. H. F.; Jones, J. Bryan
CORPORATE SOURCE: Dep. Chem., Univ. Toronto, Toronto, ON, M5S 1A1, Can.
SOURCE: Journal of the Chemical Society, Chemical Communications (1986), (20), 1545-6
CODEN: JCCCAT; ISSN: 0022-4936
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 106:210250
AB Pig liver **esterase**-catalyzed hydrolyses of variously substituted racemic allenic esters proceed with predictable enantiomeric selectivity, with the highest (93%) enantiomeric excess values being obsd. for the most highly substituted substrates. Thus, this **esterase**-catalyzed reaction is useful in resolving these racemates.

L4 ANSWER 4 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1989:113228 HCAPLUS
DOCUMENT NUMBER: 110:113228
TITLE: Optically active .alpha.-methyl-.beta.-hydroxy ester and its derivative, and their manufacture with **lipase**
INVENTOR(S): Akita, Hiroyuki; Matsukura, Hiroko; Oishi, Takeshi
PATENT ASSIGNEE(S): Institute of Physical and Chemical Research, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 19 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 63063398	A2	19880319	JP 1986-209030	19860905

PRIORITY APPLN. INFO.: JP 1986-209030 19860905
OTHER SOURCE(S): MARPAT 110:113228
AB **Lipase** is used for manuf. of optically active I (R = 2-furanyl, 2-thionyl, PhCH:CH, MeOC6H4, MeCH2CH:CH:CMeCH3, MeCH:CMeCH3, C:CMeCH3) and II (R as in I; R1 = OH) from a mixt. contg. (.+-.)-I and (.+-.)-II (R as in I; R1 = OAc), as well as the manuf. of MeCH:CMeCH3 and IV (R = 2-furanyl, 2-thionyl; R' = OH) from a mixt. contg. (.+-.)-III (R as in IV) and (.+-.)-IV (R' = OAc). Racemic I (R = 2-furanyl) 537 mg mixed with **lipase** F-Ap-15 250 mg (100 mL) was incubated at 33.degree. for 18.5 h. Optically active I (R = 2-furanyl) and II (R = 2-furanyl; R' = OH) were reacted with (+)-.alpha.-methoxy-.alpha.-trifluoromethyl phenylacetyl (MTPA) Cl 35 mg to obtain I (R = 2-furanyl)-(+)-MTPA ester 309.5 and II (R = 2-furanyl; R' = OH)-(+)-MTPA ester 44 mg having optical purity 4 and 86%, resp..

L4 ANSWER 5 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:80769 HCAPLUS
DOCUMENT NUMBER: 134:307097
TITLE: Chiral recognition of **alcohol**

enantiomers in acyl transfer reactions catalysed by Candida antarctica **lipase** B

AUTHOR(S): Orrenius, Christian; Haeffner, Fredrik; Rotticci, Didier; Ohrner, Niklas; Norin, Torbjorn; Hult, Karl

CORPORATE SOURCE: Department of Chemistry, Organic Chemistry, Royal Institute of Technology, Stockholm, S-100 44, Swed.

SOURCE: Biocatalysis and Biotransformation (1998), 16(1), 1-15
CODEN: BOBOEQ; ISSN: 1024-2422

PUBLISHER: Harwood Academic Publishers

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A description of the substrate-enzyme interactions involved in the discrimination of sec-alc. enantiomers in acyl transfer reactions catalyzed by the highly enantioselective Candida antarctica **lipase** B is presented. Exptl. found activities and enantioselectivities from kinetic resolns. of a series of secondary alc. substrates were used together with mol. modeling for the elucidation of the stereoselective substrate-enzyme interactions. Matching exptl. and calcd. results allowed conclusions regarding the orientation of the tetrahedral intermediates in the active site. The finding, valid for substrates of a specific activity above 1 .mu.mol min-1 mg-1 protein, describes the origin of enantioselectivity as a combination of a binding site of limited size, the "stereospecificity pocket", and principally different productive orientations of the two enantiomers.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1984:607103 HCAPLUS

DOCUMENT NUMBER: 101:207103

TITLE: **Lipase**-catalyzed hydrolysis as a route to esters of chiral epoxy alcohols

AUTHOR(S): Ladner, Wolfgang E.; Whitesides, George M.

CORPORATE SOURCE: Dep. Chem., Harvard Univ., Cambridge, MA, 02138, USA

SOURCE: Journal of the American Chemical Society (1984), 106(23), 7250-1
CODEN: JACSAT; ISSN: 0002-7863

DOCUMENT TYPE: Journal

LANGUAGE: English

OTHER SOURCE(S): CASREACT 101:207103

AB Hydrolysis of racemic esters of epoxy alcs., e.g., esters of glycidol (or its derivs.) with alkanoic acids, catalyzed by porcine pancreatic **lipase** (EC 3.1.1.3), proceeds with useful enantioselectivity, causing the selective hydrolysis of 1 of the enantiomers. A representative procedure shows that hydrolysis of racemic glycidyl butyrate by **lipase** yields (R)-glycidyl butyrate in .apprx.100-g quantities with enantiomeric excess >92%. **Lipase** is not deactivated by reaction with the epoxide moiety, and it hydrolyzes a wide variety of structures. It is active at H2O-org. interfaces, and soly. of the org. substrate in H2O is not necessary. The enantioselectivity depends on the structure of the acid components of the ester, and better results are obtained with longer n-alkyl groups up to pentyl; then foaming and emulsification becomes an exptl. problem.

L4 ANSWER 7 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1994:597246 HCAPLUS

DOCUMENT NUMBER: 121:197246

TITLE: Development of a new Bacillus carboxyl **esterase** for use in the resolution of chiral drugs

AUTHOR(S): Quax, W. J.; Broekhuizen, C. P.

CORPORATE SOURCE: Gist-brocades BV, Delft, 2611 XT, Neth.

SOURCE: Applied Microbiology and Biotechnology (1994), 41(4), 425-31
CODEN: AMBIDG; ISSN: 0175-7598

DOCUMENT TYPE: Journal
LANGUAGE: English

AB The authors have screened a new enzyme for the resoln. of R,S-naproxen enantiomers. The enzyme is free of **lipase** activity, and possesses a very high stereospecificity on S-naproxen [2-(6-methoxy-2-naphthyl)propionic acid] esters and esters of related drugs. The primary structure of the enzyme, detd. from the nucleotide sequence, shows limited homol. with the catalytic site of **lipases**. The gene coding for the stereoselective carboxylesterase has been cloned and expressed in Bacillus subtilis. Using a multicopy vector and an addnl. strong promoter an efficient prodn. process was developed. The enzyme was shown to be sensitive to very high concns. of the products formed during the reaction it catalyzes. To increase the resistance of the enzyme, lysine residues thought to be responsible for this phenomenon were replaced through site-directed mutagenesis. Enzymes with improved stability were obtained. An explanation is given in terms of a model in which a reaction of the acid moiety of naproxen with free lysine NH2 groups is a major cause of inactivation.

L4 ANSWER 8 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1994:577857 HCAPLUS
DOCUMENT NUMBER: 121:177857
TITLE: Enzymic process for the stereoselective preparation of a hetero-bicyclic **alcohol enantiomer**
.
INVENTOR(S): Buizer, Nicolaas; Kruse, Chris G.; van der Laan, Melle; Langrand, Georges; van Scharrenburg, Gustaaf J. M.; Snoek, Maria C.
PATENT ASSIGNEE(S): Duphar International Research B.V., Neth.
SOURCE: Eur. Pat. Appl., 20 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 605033	A1	19940706	EP 1993-203451	19931209
EP 605033	B1	19990721		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
AT 182367	E	19990815	AT 1993-203451	19931209
EP 939135	A1	19990901	EP 1998-204281	19931209
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE				
ES 2134241	T3	19991001	ES 1993-203451	19931209
ZA 9309435	A	19940809	ZA 1993-9435	19931215
CA 2111607	AA	19940622	CA 1993-2111607	19931216
FI 9305676	A	19940622	FI 1993-5676	19931216
NO 9304652	A	19940622	NO 1993-4652	19931216
HU 67694	A2	19950428	HU 1993-3619	19931216
HU 213569	B	19970828		
RO 112517	B1	19971030	RO 1993-1714	19931216
CZ 286077	B6	20000112	CZ 1993-2784	19931216
AU 9352502	A1	19940630	AU 1993-52502	19931217
AU 674547	B2	19970102		
JP 06237790	A2	19940830	JP 1993-343229	19931217
CN 1101378	A	19950412	CN 1993-121130	19931217
CN 1054882	B	20000726		
PL 177831	B1	20000131	PL 1993-301539	19931217
PL 178517	B1	20000531	PL 1993-332294	19931217
TW 381120	B	20000201	TW 1993-82110748	19931218
IL 108090	A1	19981030	IL 1993-108090	19931220
RU 2124506	C1	19990110	RU 1993-55675	19931220
CN 1160714	A	19971001	CN 1997-101035	19970122
US 5914263	A	19990622	US 1997-899155	19970723

CZ 286162	B6	20000112	CZ 1997-2905		19970915
CN 1255496	A	20000607	CN 1999-121080		19991006
GR 3031446	T3	20000131	GR 1999-402535		19991007
PRIORITY APPLN. INFO.:			EP 1992-204043	A	19921221
			EP 1993-203451	A3	19931209
			US 1993-167084	A3	19931216

AB The invention relates to an enzymic process for the stereoselective prepn. of a hetero-bicyclic alc. enantiomer, characterized in that a substantially pure enantiomer (I) (X = O, S, NH, N-(C1-C4) alkyl or CH2; Y1, Y2 and Y3 are each independently hydrogen or substituents selected from halogen, C1-C4 alkyl, C1-C4 alkoxy, C1-C4 haloalkyl, nitro and cyano; the NO2 substituent is attached to the bicyclic ring system in the 5- or 7-position; and the C*-atom has either the R or the S configuration) is prepd. from its corresponding alc. racemate by the following successive reactions steps: (1) stereoselective esterification, (2) sepn. of the alc. from the ester produced, (3) hydrolysis of said ester to produce the corresponding alc. enantiomer, and (4) conversion of said alc. enantiomer into the starting racemate under basic conditions to allow its reuse. The invention also relates to a substantially pure alc. enantiomer I, to the use of said enantiomer for the prepn. of a pharmacol. active piperazine deriv. (II; A = straight or branched C2-4 alkylene; B = Ph or heterocyclic group selected from thienyl, pyranyl, furyl, etc.; X and Y are described above) and to substantially pure enantiomeric intermediates.

L4 ANSWER 9 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1999:281784 HCAPLUS
TITLE: Chiral discrimination of cyclic 1,3-amino **alcohol enantiomers**
AUTHOR(S): Peter, Maria; Bernath, Gabor; Fulop, Ferenc; Van Der Eycken, Johan
CORPORATE SOURCE: Szent-Gyorgyi Albert Orvostudomanyi Egyetem, Gyogyszerkemiai Intezet, Szeged, 6720, Hung.
SOURCE: Magyar Kemiai Folyoirat (1999), 105(2), 61-70
CODEN: MGKFA3; ISSN: 0025-0155
PUBLISHER: Magyar Kemikusok Egyesulete
DOCUMENT TYPE: Journal
LANGUAGE: Hungarian

AB Racemic 1,3-amino alcs. were resolved via **lipase**-catalyzed O-acylation of their Z derivs., using vinyl butyrate in different ethers as solvents. In accordance with the empirical rule, most of the screened **lipases** preferred the 1S enantiomer. In order to monitor the enzymic reactions a high-performance liq. chromatog. method was developed. The applied chiral stationary phase (Chiralcel OD) allowed simultaneous sepn. of all the four isomers which were present in the reaction mixt. Retention mechanisms of alc. and ester analogs were investigated in detail. Besides the direct way, indirect sepn. involving precolumn derivatization with 1-fluoro-2,4-dinitrophenyl-5-L-alaninamide permitted the differentiation of 1,3-amino alc. enantiomers with high resoln. In combination with the addn. of stds., both direct and indirect methods can be used to identify abs. configurations and hence to det. the enzyme selectivity.

L4 ANSWER 10 OF 37 HCAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1991:120946 HCAPLUS
DOCUMENT NUMBER: 114:120946
TITLE: Enzyme-catalyzed reactions. 7. Enantioselective esterification of racemic cyanohydrins and enantioselective hydrolysis or transesterification of cyanohydrin esters by **lipases**
AUTHOR(S): Effenberger, Franz; Gutterer, Beate; Ziegler, Thomas; Eckhardt, Elisabeth; Aichholz, Reiner
CORPORATE SOURCE: Inst. Org. Chem., Univ. Stuttgart, Stuttgart, D-7000/80, Germany
SOURCE: Liebigs Annalen der Chemie (1991), (1), 47-54
CODEN: LACHDL; ISSN: 0170-2041

DOCUMENT TYPE: Journal
LANGUAGE: German
OTHER SOURCE(S): CASREACT 114:120946

AB Pure cyanohydrin enantiomers (S)- and (R)-HOCHRCN [R = Pr, Ph, phenethyl, benzo[1,3]dioxol-5-yl, 3,4-MeO(HO)C6H3] and their O-acyl derivs. are obtained from three different **lipase**-catalyzed reactions: i) enantioselective hydrolysis of aliph. and arom. racemic cyanohydrin esters, ii) enantioselective acylation of racemic cyanohydrins, and iii) enantioselective transesterification of esters with primary alcs. Both the cyanohydrin esters and the free cyanohydrins (which are prone to racemization) are isolated as enantiomers with high optical purity on a preparative scale. Hydrolysis of the racemic butyrates with candida cylindracea **lipase** and pseudomonas sp. **lipase**, resp., for example, affords (S)-I (R = Pr, Ph) in high yield with 97 and 96% ee, resp. (S)-I (R = Pr) is obtained with the same optical purity by candida sp. **lipase**-catalyzed transesterification of PrCO2CHPrCN with 1-octanol.

=> FIL STNGUIDE

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	51.48	51.69

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-8.25	-8.25

FILE 'STNGUIDE' ENTERED AT 15:33:55 ON 24 APR 2006
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 21, 2006 (20060421/UP).

=> d his

(FILE 'HOME' ENTERED AT 15:25:35 ON 24 APR 2006)

FILE 'MEDLINE, HCAPLUS, BIOSIS' ENTERED AT 15:26:02 ON 24 APR 2006
L1 1 S ANTI-KAZLAUSKAS LIPASE
L2 41 S (LIPASE? OR ESTERASE?) AND (ESTER ENANTIOMER? OR ALCOHOL ENAN
L3 37 DUP REM L2 (4 DUPLICATES REMOVED)
L4 37 FOCUS L3 1-

FILE 'STNGUIDE' ENTERED AT 15:33:55 ON 24 APR 2006

=> s l4 and kazlauskas
L4 CANNOT BE SEARCHED IN STNGUIDE
The L-number cannot be used because it does not contain a query.
Enter DISPLAY HISTORY to see the sequence of commands that created this L-number.

=> file medline hcaplus biosis

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.36	52.05

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-8.25

FILE 'MEDLINE' ENTERED AT 15:37:31 ON 24 APR 2006

```
FILE 'HCAPLUS' ENTERED AT 15:37:31 ON 24 APR 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOSIS' ENTERED AT 15:37:31 ON 24 APR 2006
Copyright (c) 2006 The Thomson Corporation

=> s kazlauskas and l4
L5            0 KAZLAUSKAS AND L4

=> s l4 and kazlauskas
L6            0 L4 AND KAZLAUSKAS

=> s l4 and anti-kazlauskas
L7            0 L4 AND ANTI-KAZLAUSKAS

=> d his

     (FILE 'HOME' ENTERED AT 15:25:35 ON 24 APR 2006)

     FILE 'MEDLINE, HCAPLUS, BIOSIS' ENTERED AT 15:26:02 ON 24 APR 2006
L1             1 S ANTI-KAZLAUSKAS LIPASE
L2            41 S (LIPASE? OR ESTERASE?) AND (ESTER ENANTIOMER? OR ALCOHOL ENAN
L3            37 DUP REM L2 (4 DUPLICATES REMOVED)
L4            37 FOCUS L3 1-

     FILE 'STNGUIDE' ENTERED AT 15:33:55 ON 24 APR 2006

     FILE 'MEDLINE, HCAPLUS, BIOSIS' ENTERED AT 15:37:31 ON 24 APR 2006
L5             0 S KAZLAUSKAS AND L4
L6             0 S L4 AND KAZLAUSKAS
L7             0 S L4 AND ANTI-KAZLAUSKAS

=> log
ALL L# QUERIES AND ANSWER SETS ARE DELETED AT LOGOFF
LOGOFF? (Y)/N/HOLD:y
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                  ENTRY    SESSION
FULL ESTIMATED COST                                3.79      55.84

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)      SINCE FILE      TOTAL
                                                  ENTRY    SESSION
CA SUBSCRIBER PRICE                                0.00      -8.25

STN INTERNATIONAL LOGOFF AT 15:39:07 ON 24 APR 2006
```